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Association between inflammatory cytokines and other Biochemical parameters in patients after 48 hrs of first myocardial infarction (MI)

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***Abstract*— Myocardial infarction (MI) is a term used to describe a heart attack that occurs when blood flow to the heart muscle reduced, and plaque builds up in the lining of the coronary arteries, resulting in insufficient oxygen supply. The study was conducted on a number of participants, including 100 cases and 70 controls, who were matched for gender and age. The blood indicators in question were examined using standard laboratory techniques and equipment. The study aimed to study the relationship between inflammatory cytokines, lipid profiles, and transaminase enzyme in patients 48 hours after myocardial infarction. The results indicated that there are differences between cases and controls for inflammatory cytokines (IL-8, IL-12, and IFN-A*α*). Moreover, total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were decreased in cases in comparison with controls, while triglyceride (TG) was high in patients after MI. However, patients' aspartate transaminase (AST) levels were meaningfully higher than in controls.**

***Keywords*— Inflammatory cytokines, myocardial infraction, lipid profile, transaminase enzyme.**

I. INTRODUCTION

The term "myocardial infarction" (MI) refers to the presence of acute myocardial injury, as indicated by an unusual biomarker of the heart that is thought to be an indicator of acute myocardial injury (Thygesen *et al.*, 2018). MI occurs due to the reduced flow of blood to the heart myocardium and the rarity of oxygen supply (Lu *et al.*, 2015). MI is regarded as one of the top causes of death and disability worldwide (Thygesen *et al.*, 2012). Mediators of myocardial inflammation, primarily cytokines, have been involved in curing after infarction for many years. Recently, however, the possibility that inflammation may lead to harmful complications of myocardial infarction has received an increasing attention. Pro-inflammatory cytokines can interfere with myocardial dysfunction linked to myocardial infarction (Sharma *et al.*, 1997).Myocardial infarction (MI) is a significant worldwide health issue that contributes to high morbidity and death worldwide, despite new scientific and technical research and evidence to the contrary. Poor results in the healing process of post-MI wounds and maladaptive left ventricular remodeling are linked to unchecked immune-inflammatory pathways.. Given the involvement of immune cells in the host response versus tissue injury, understanding the relevant cellular subsets, origins, and functions is critical for revealing novel therapeutic techniques that maintain the protective immune system and promote optimal healing (Anzai *et al.*, 2022). Also, it has been known that MI pathogenesis is multifactorial. According to some reports, Impaired lipid metabolism is one of the key factors in developing MI (Kumar *et al.*, 2009 , Kulsoom *et al.*, 2006).

AST is involved in a variety of amino acid metabolisms. It regulates the NAD+/NADH ratio in cells, the activity of the Krebs cycle, the combination of purine/pyrimidine bases, urea, protein synthesis, and gluconeogenesis. The action of AST is greatly handed out across the tissues of humans, with the most significant activity elevation in the heart, kidney, skeletal muscle, brain, and liver. The high activity of AST may be due to the damage of tissue, increased tissue expression, and plasma membrane bleb formation. Also, Serum AST activity rises proportionally to the extent of MI in patients with acute myocardial infarction (Ndrepepa, 2021). Examining the changes in MI patients after 48 hours was the primary goal of the current investigation. We examined aspartate-transaminase, IL-8, IL-12, and IFN-A levels to explore the connection between lipid profile and inflammation (AST).

I. MATERIALS AND METHODS

A. Study design

First, There were 100 cases after 48 hrs of first myocardial infarction (MI), and 70 normal cases (Healthy group). There were 67 male and 33 female patients with first MI, with a mean age of 65± 6.6 years. Age, gender, and body mass index (BMI) were matched for cases in all patients as indicated in Table (1).

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TABLE I. CHARACTERISTICS OF THE STUDY DESIGN AND POPULATION. PATIENTS AND HEALTHY GROUP ARE MATCHED FOR AGE, GENDER, AND BMI. THERE WAS A SIGNIFICANT DIFFERENCE IN SMOKING HABITS, ARTERIAL HYPERTENSION BETWEEN PATIENTS, AND HEALTHY GROUP

	First myocardial infarction (MI) cases	***Healthy cases***	***P value***
N	100	70	-
Male	67	41	<0.05
Female	33	29	<0.05
Mean age (years)	65± 6.6	61± 4.0	0.102
Body mass index (Kg/m^2)	25.66 ± 5.91	23.55 ± 6.32	0.143
Diabetes mellitus	18	13	0.124
Smoking	58	22	0.049
Hypertension	63	56	0.048

[a.] Sample of a Table footnote. (*Table footnote*)

B. Methods

Laboratory measurements: Blood was drawn from each subject in serum separator tubes after an overnight fast and two days of MI. The serum from each patients was separated from the blood and stored at -20 °C using a centrifuge set at 3000 xg.

On day two after MI, pro-inflammatory markers in blood serum were assessed. Human IL-8 / CXCL8 ELISA Kit, human IL-12 p70 ELISA Kit, and human IFN Alpha ELISA were utilized, respectively, to measure the interleukins IL-8, IL-12, and serum concentrations.

The Hitachi 704 Analyzer, which Roche Diagnostics maintains, was used to determine total cholesterol, lipoproteins, and triglycerides levels (the serum lipid profile). The Sigma-Aldrich determined serum AST concentrations using Aspartate Aminotransferase (AST) Activity Assay Kit.

C. Statistical analysis

Analysis of variance was used to find differences between patients groups in terms of inflammatory biomarkers, serum AST levels, and lipid profiles. The results were expressed in terms of ± mean, standard deviation (SD), with p values <0.05 were considered significant.

III. RESULTS

As presented in Table 1, there it can be observed that there are a significant differences in smoking habits, arterial hypertension between patients and control groups. All patients, after 48 hrs of first myocardial infarction (MI), demonstrated elevated levels of pro-inflammatory markers (IL- 8, IL- 12, and IFN-α). However, in contrast to the control group, these changes were more pronounced, as seen in Table 2. Negative side effects from myocardial infarction could be brought on by the inflammation. Pro-inflammatory cytokines can intercede myocardial dysfunction linked to myocardial infarction.

The present results data on triglyceride concentrations, which involved 100 participants vs. 70 control, showed a significant elevation in serum TG in MI cases after 48 hours in comparison with the control group, as illustrated in Table 2., On the other hand, while there was an important decrease in serum TC, LDL, and HDL. Also our results showed that hat the study group's AST levels were greater than those of the control group, (Table 2).

TABLE II. THE LEVELS OF INFLAMMATORY MARKERS, LIPID PROFILE AND ASPARTATE- TRANSAMINASE IN SERUM SAMPLE OF MI PATIENTS AND HEALTHY

Parameters	***(MI) cases (n=100)***	***Healthy cases (n=70)***
IL-8 (pg/mL)	11.96±5.73[a*]	4.21± 0.16
IL-12 (pg/mL)	40.66±12.10[*]	23.95±2.25
IFN-α (pg/mL)	453.24±13.80 [*]	187.89±10.19
TC (mmol/dL)	1.09±4.42[*]	4.50±0.21
LDL (mmol/L)	1.14±4.27[*]	3.34±0.07
HDL (mmol/dL)	0.65±1.30[*]	1.07±0.13
TG (mmol/L)	22.32±8.89[*]	0.93±0.27
AST (IU/L)	57.78±10.16[*]	20.56±11.98

[a.] Values are given as mean ± SD. P ≤ 0.05, * significantly different from control

IV. DISCUSSION

As presented in Table 1, there can be observed a significant difference in smoking habits, arterial hypertension between patients and Healthy group. All patients, after 48 hrs of first myocardial infarction (MI), demonstrated elevated levels of pro-inflammatory markers (IL- 8, IL- 12, and IFN-α). In contrast to the Healthy group , these changes were more pronounced, as seen in Table 2. Negative side effects from myocardial infarction could be brought on by the inflammation. Pro-inflammatory cytokines can intercede myocardial dysfunction linked to myocardial infarction.

Many different cytokines can be found in abundance in inflammatory cells that can be lethal to heart muscle cells. At the cellular level, it has been shown that the deficiency in the amount of oxygen reaching the tissues leads to a chain of well-attested changes in the cells of heart muscles that involve lack of contractility, lipid metabolism changes, and irreversible damage of the cell membrane, which leads to the death of the cell (Sharma *et al.*, 1997)

Inflammatory responses and cytokine production are highly active during a myocardial infarction, which helps with heart (cardiac) remodeling and the final host prognosis. Mechanical deformation, ischemia stimulation, reactive oxygen species (ROS), and cytokine self-amplification pathways are among the factors that cause cytokine production in the acute post-infarction period (Nian, 2004). (Ellis *et al.*, 2019) found that IFN-α application on Male Wistar rats worsened ventricular dilatation and grew infarct size at day 28 after-MI. Additionally, at day 3 after MI,

IFN-α enhanced the presence of the alternative macrophage subset in the myocardium while shifting the distribution of peripheral monocyte subsets toward the pro-inflammatory monocyte subset.

(Chen *et al.,* 2020) reported that an elevated level of IFN-α in serum is linked to cardiovascular disease, which affects plaque-residing macrophages, and leads to triggering atherosclerosis. Due to its crucial role in post-infarction inflammation, high levels of circulating IL-8 have been linked to large infarct sizes, impaired recovery of left ventricular function, and poor clinical outcomes in patients with acute ST-segment elevation myocardial infarction. This suggests IL-8 as a potential therapeutic target in the future (Shetelig *et al.,* 2018).

According to (Ye *et al.,* 2020) cytokines are crucial in the emergence of heart disorders. IL-12 family members are a type of cytokine that regulates a diversity of effects of biology; they are linked to the progression of numerous cardiovascular diseases, as myocardial infarction. The present data on triglyceride concentrations, which involved 100 participants vs. 70 control, showed a significant elevation in serum TG in MI cases after 48 hours in comparison with the Healthy group , as illustrated in Table 2, while there was an important decrease in serum TC, LDL, and HDL. (Khan *et al.,* 2013) compared the lipid profiles (serum TC, LDL, HDL, and triglycerides (TG)) in 67 AMI patients and found a major decrease in TC, LDL, and HDL levels in AMI patients.

(Jiao *et al.,* 2018) found that populations with a BMI >25 kg/m2 and an age of ≥ 65 years old are more likely to get MI due to high fast. MI is referred to as a severe phase response. levels of Lipid and lipoprotein vary after acute MI within (24 – 48) h after the start of chest pain. Major post-infarction decreases in TC occur on the fourth to fifth days; LDL and HDL reduce to their lowest levels on day 7. The levels of TG rise after acute MI to the highest level on day 7. Lipid and lipoprotein levels usually return to normal within 2 months of an acute MI (Robert, 1993). Also, (Gaziano *et al.,* 1999) noted that the mean TC and LDL concentrations were meaningfully reduced when compared to approximately two to three months later. TC and LDL concentrations decrease after an acute MI. (Kumar *et al.,* 2019) evaluated the change in serum lipid profile in AMI and found that the mean serum total cholesterol (TC) levels decreased after 48 hours, while mean serum triglyceride (TG) levels were increased and mean serum low-density lipid-cholesterol (LDL-C) and high-density lipid-cholesterol (HDL-C) were decreased.

The results of the present study showed that hat the study group's AST levels were greater than those of the control group. Table 2 agrees with the study of (Shamshirian *et al.,* 2020), which found that AST levels were meaningfully higher in patients with MI, and the risk of MI was approximately 24 times higher in cases with high AST levels than in the control group.

(Li *et al.,* 2021) investigated the predictive value of AST in AMI patients for mortality. They looked into how well the AST predicted mortality in AMI patients. AST levels differed significantly between ST-segment elevation and non-ST-segment elevation myocardial infarction.

Acute myocardial infarction (AMI) mortality has not been shown, despite the fact that AST has been associated with an elevated risk of cardiovascular disease. Myocardial tissue damage is accompanied by an increase in enzyme serum levels of AST as a result of myocardial cellular damage. According to (Morrow *et al.,* 2007) patients with acute, first-ever MI had mean peak serum AST levels that were noticeably greater than controls.

V. CONCLUSION

Finding the alterations in mi patients after 48 hours was the goal of our investigation. We also assessed The levels of the inflammatory markers IL-8, IL-12, and IFN- along with the levels of aspartate-transaminase was also assessed to investigate the relationship between lipid profile and inflammation (AST). Significant differences can be observed in pro-inflammatory markers (IL- 8, IL- 12, and IFN-α); myocardial enzyme serum (AST) levels increased within 48 hours of mi. After 48 hours, there was an essential rise in serum TG in mi patients compared to the control group, although TC), LDL), and HDL levels significantly decreased. The results of this study supported the need for estimating inflammatory markers, lipid profiles, and AST levels in MI patients right away after myocardial infarction occurs to identify people who may be at a higher risk.

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REFERENCES

1. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD. Fourth universal definition of myocardial infarction. J Am Coll Cardiol. 2018;72(18):2231-2264.

2. Lu L, Liu M, Sun R, Zheng Y, Zhang P. Myocardial Infarction: Symptoms and Treatments. Cell Biochem Biophys. 2015;72(3):865-867.

3. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. Circulation. 2012;126(16):2020-2035.

4. Sharma HS, Das DK. Role of cytokines in myocardial ischemia and reperfusion. Mediators Inflamm. 1997;6(3):175-83.

5. Anzai, A.; Ko, S. Fukuda, K. Immune and Inflammatory Networks in Myocardial Infarction: Current Research and Its Potential Implications for the Clinic. Int. J. Mol. Sci. 2022; 23: 5214.

6. Kumar A, Nagtilak S, Sivakanesan R, Gunasekera S. Cardiovascular risk factors in elderly normolipidemic acute myocardial infarct patients-a case controlled study from India. Southeast Asian J Trop Med Public Health. 2009;40:581–92.

7. Kulsoom B, Nazrul SH. Association of serum C-reactive protein and LDL:HDL with myocardial infarction. J Pak Med Assoc. 2006;56:318–22.

8. Ndrepepa G. Aspartate aminotransferase and cardiovascular disease—a narrative review. J Lab Precis Med 2021;6:6.
9. Nian M. Inflammatory Cytokines and Postmyocardial Infarction Remodeling. Circulation Research. 2004; 94(12): 1543–1553.
10. ter Horst, Ellis N.; Krijnen, Paul A. J.; Hakimzadeh, Nazanin; Robbers, Lourens F. H. J.; Hirsch, Alexander; Nijveldt, Robin; Lommerse, Ingrid, et al. Elevated monocyte-specific type I interferon signaling correlates positively with cardiac healing in myocardial infarct patients but interferon alpha application deteriorates myocardial healing in rats. Basic Research in Cardiology. 2019; 114(1): 1–12.
11. Chen, Hung-Jen; Tas, Sander W.; de Winther, Menno P.J. Type-I interferons in atherosclerosis. Journal of Experimental Medicine.2020; 217(1): e20190459–. doi:10.1084/jem.20190459.
12. Shetelig, Christian; Limalanathan, Shanmuganathan; Hoffmann, Pavel, et al. Association of IL-8 With Infarct Size and Clinical Outcomes in Patients With STEMI. Journal of the American College of Cardiology. 2018; 72(2): 187–198.
13. Ye J, Wang Y, Wang Z, et al. Roles and Mechanisms of Interleukin-12 Family Members in Cardiovascular Diseases: Opportunities and Challenges. Front Pharmacol. 2020;11:129.
14. Khan HA, Alhomida AS, Sobki SH. Lipid profile of patients with acute myocardial infarction and its correlation with systemic inflammation. Biomark Insights. 2013;8:1-7.
15. Jiao ZY, Li XT, Li YB, Zheng ML, Cai J, Chen SH, Wu SL, Yang XC. Correlation of triglycerides with myocardial infarction and analysis of risk factors for myocardial infarction in patients with elevated triglyceride. J Thorac Dis 2018;10(5):2551-2557.
16. Robert S. Rosenson. Myocardial injury: The acute phase response and lipoprotein metabolism. 1993; 22(3): 933–940.
17. Gaziano JM, Hennekens CH, Satterfield S, Roy C, Sesso HD, Breslow JL, Buring JE. Clinical utility of lipid and lipoprotein levels during hospitalization for acute myocardial infarction. Vasc Med. 1999;4(4):227-31.
18. Kumar N, Kumar S, Kumar A, Shakoor T, Rizwan A. Lipid Profile of Patients with Acute Myocardial Infarction (AMI). Cureus. 2019; 11(3): e4265. https://doi:10.7759/cureus.4265.
19. Shamshirian A, Navaei RA, Abedi S. Levels of Blood Biomarkers among Patients with Myocardial Infarction in Comparison to Healthy group . Ethiop J Health Sci. 2020;30(1):5.doi:http://dx.doi.org/10.4314/ejhs.v30 i1.2
20. Li J, Zhao Z, Jiang H, Jiang M, Yu G, Li X. Predictive value of elevated alanine aminotransferase for in-hospital mortality in patients with acute myocardial infarction. BMC Cardiovasc Disord. 2021; 21, 82. https://doi.org/10.1186/s12872-021-01903-z.
21. Morrow DA, Cannon CP, Jesse RL, Newby LK., Ravkilde J, Storrow AB, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Characteristics and Utilization of Biochemical Markers in Acute Coronary Syndromes. Circulation. 2007; 115.